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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KIM, YOUNG J	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 06/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/036,729	MIDDELDORP ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-9,23 and 25-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-9,23 and 25-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/031,148.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The instant Office Action is responsive to the Amendment received on March 24, 2005.

Preliminary Remark

The Office acknowledges the addition of claims 32-34, in the Amendment received on March 24, 2005.

With regard to claims 7, 8, and 32-34, reciting the phrase, "the nucleic acid sequence ***as shown in SEQ ID NO:***..." (emphasis added), Applicants are suggested to use non-ambiguous and most commonly used phrase, "the nucleic acid ***comprising*** SEQ ID NO:" The phrase, "nucleic acid as shown in," could result in ambiguity as to whether the nucleic acid comprises the recited SEQ ID Number or a part of the SEQ ID Number.

Claim Interpretation

The claim interpretation with regard to claim 34, drawn to the embodiment of a nucleic acid comprising the nucleic acid sequence as shown in SEQ ID NO: 1 or a subsequence thereof, wherein said subsequences encodes an Epstein-Barr Virus peptide comprising the combination of the amino acid sequence of SEQ ID NO: 5 or SEQ ID NO: 6, is determined to be a nucleic acid encoding the whole peptides (peptides 3 and 4) that are linked adjacently to each other (based on pages 22 and 34 of the instant specification). In other words, the claim would not embrace a nucleic acid encoding a peptide comprising a combination of peptide SEQ ID NO: 5 or 6, wherein said peptide comprises combination produced from a sub-segment of SEQ ID NO: 5 and a sub-segment of SEQ ID NO: 6.

Claim Rejections - 35 USC § 112

The rejection of claims 23, 28, and 29 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, made in the Office Action mailed on December 27, 2004 is withdrawn in view of the Amendment received on March 24, 2005.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

- Maintained -

The rejection of claims 6-9, 25-27, 30, and 31 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, made in the Office Action mailed on December 27, 2004 is maintained for the reasons of record.

Applicants' arguments presented in the Amendment received on March 24, 2005 have been fully considered but they are not found persuasive for the following reasons.

Applicants' arguments are addressed in the same order they were presented.

It should be made clear that the rejection had been made under the first paragraph of the 35 U.S.C.[1]

Applicants state that claim 6, as currently amended, is drawn to an isolated nucleic acid sequence encoding:

a) a peptide immunochemically reactive with antibodies to the EBV VCA-p18 or VCA-p40 proteins, comprising an *immunoreactive fragment* of the VCA-p18 or VCA-p40 protein, encoded within the EBV open reading frame BFRF3 and BdRF1, respectively; or

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[1] On page 6 of the Applicants' response, Applicants state that claims 6-9, 23, and 25-31 were rejected under 35 U.S.C. 112, *second* paragraph.

b) a *functional variant* of said peptide described in a, wherein said variant is immunochemically reactive with antibodies to the EBV virus VCA-p18 or VCA-p40 proteins.

Applicants contend that due to the amendment, claim 6 would define a *genus* of nucleic acids that encode peptides comprising an immunoreactive fragment of the VCA-p18 or VCA-p40 protein of EBV or functional variants thereof, all of which are immunoreactive with antibodies specific to VCA-p18 or VCA-p40 proteins, thus rendering the claim to ***not*** include a nucleic acid that encode ***any*** polypeptide that is reactive with ***any*** antibodies to EBV (page 7, 2nd and 3rd paragraph, Response).

In response, claim 6 is embraces two different embodiment:

Embodiment A) is drawn to a nucleic acid encoding ***any*** peptide that is reactive with antibodies which are reactive to VCA-p18 or VCA-p40 proteins, said ***any*** peptide comprising an immunoreactive fragment of the VCA-p18 or VCA-p40 proteins.

Thus, claim embraces any nucleic acid that encodes at least a fragment of a protein (which is one residue) that is in common with the VCA-p18 or VCA-p40 proteins, and said protein reacts with the recited antibody. Hence, if the antibody is a human antibody, said antibody would react with any protein that is from sources other than human, effectively embracing any nucleic acid encoding any protein, wherein the source of the protein is other than that which the antibody is generated/isolated from. Clearly, Applicants do not have a representative number of species to demonstrate possession of the genus embraced by this claim.

Embodiment B) is drawn to a functional variant of the above nucleic acid, which would fail under the same reasoning as the above. In addition, neither the Applicants nor one of skill in the art would be able to distinguish what nucleic acids are embraced by the instant claims

because the neither would know from which of the plurality of nucleic acids are functional variants, wherein the function is unknown.

Claims 7 and 8 would fail to provide sufficient written description for the same reason.

While claims 7 and 8 are drawn to a nucleic acid sequence comprising SEQ ID NO: 1 and 3 (respectively) or a *subsequence thereof*, wherein said subsequence encodes an EBV peptide comprising an *epitope* that is immunochemically reactive with antibodies to the EBV VCA-p18 protein, as already discussed above, any nucleic acid encoding a protein that is not from the same source from which the claimed antibody is generated/produced, would necessarily react with said antibody, thus inherently demonstrating the presence of an epitope. The limitation, "Epstein-Barr Virus peptide," found in claims 7 and 8 are determined to be met so long as a peptide reacts with the claimed antibody.

Additionally, claim 8, which is drawn to an isolated nucleic acid comprising SEQ ID NO: 3, *or a subsequence thereof*, wherein said subsequence encodes an EBV peptide comprising an epitope that is immunochemically reactive with antibodies to EBV VCA-p40 protein lacks written description.

While the instant specification has SEQ ID NO: 3 (VCA-p40 coding sequence) as originally filed, the specification absolutely fails to disclose a reasonable number of epitopes within VCA-p40 protein which are found to be immunochemically reactive with antibodies, thus failing to describe that Applicants were in possession of nucleic acid fragments that encode such epitopes.

Claims 9, 26, and 27 drawn to a vector comprising such nucleic acids would also fail as such nucleic acids have not been sufficiently described.

Claims 25, 30, and 31 would fail under the same reason. To expound, the claims are drawn to a kit for detecting the presence of an EBV in a sample, wherein the intended use limitation are not given any patentable weight. Hence, the kit effectively comprises a set of primers according to the above nucleic acids which already have been discussed above as lacking written description, also rendering the kit lacking written description. It should also be noted that an embodiment of the kit is drawn to a primer that not only comprises the nucleic acids discussed above, but also a fragment of said nucleic acids. Additionally, the phrase recited the reagents *for amplification/detection* are also not given any patentable weight since any reagent, buffers, labeled dyes, would be useful in said detection/amplification.

In a decision regarding *University of California v. Eli Lilly and Co.*, CAFC 43 USPQ2d 1398 (7/22/1997), a patent claim drawn to a microorganism containing a human insulin cDNA was determined to ***lack*** proper written description even though the specification provided a rat cDNA encoding insulin along with general description of obtaining a human insulin (at 1406).

In addition, the court further determined that a generic claim drawn to a cDNA encoding mammalian insulin also ***lacked*** proper written description even though at least one species (rat cDNA) embraced by the genus was described in the specification (at 1406).

Hence, it is clear that claims drawn to a broad genus of any nucleic acid encoding any protein so long as it reacts with a particular antibody are not properly described.

With regard to Applicants' arguments drawn to the similar language being found on a U.S. Patent, every application is examined according to its own merits, and hence, is not found persuasive.

- New Grounds – Necessitated by Amendment -

Claims 32-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

Claim 32 is drawn to an isolated nucleic acid comprising SEQ ID NO: 1, *or a subsequence thereof*, wherein said subsequence encodes a peptide comprising *at least* 12 contiguous amino acids of EBV VCA-p18 protein, wherein said peptide comprises an epitope that is immunochemically reactive with antibodies to EBV VCA-p18 protein.

The instant specification provides description for SEQ ID NO: 1, and the instant specification provides description of 11 species of 12-mers from VCA-p18 protein which are immunochemically reactive with the antibody to EBV VCA-p18 (Table 1, page 32, instant specification), the specification absolutely fails to have written description basis for the limitation, "***at least*** 12 contiguous amino acids," as the specification only provides for a specific length and not something that is greater than nucleic acid fragments encoding peptides which are immunochemically reactive and are longer than 12 amino acids in length.

Claim 33 is drawn to an isolated nucleic acid comprising SEQ ID NO: 3, *or a subsequence thereof*, wherein said subsequence encodes a peptide comprising at least 12 contiguous amino acids of EBV VCA-p40 protein, wherein said peptide comprises an epitope that is immunochemically reactive with antibodies to EBV VCA-p40 protein.

While the instant specification has SEQ ID NO: 3 as originally filed, the specification absolutely fails to demonstrate that Applicants contemplated a nucleic acid fragment that encodes any 12-mers of VCA-p40 protein. Applicants have neither isolated any protein fragments that are 12-mers of VCA-p30 protein, said proteins being immunochemically reactive with the antibody to EBV VCA-p40 protein, nor any nucleic acid fragments of 36-mers of SEQ ID NO: 3.

Claim 34 recites the below:

An isolated nucleic acid sequence, comprising the nucleic acid sequence as shown in SEQ ID NO: 1 or a subsequence thereof, wherein said subsequence encodes an Epstein-Barr Virus peptide comprising the amino acid sequences of SEQ ID NO: 5 or SEQ ID NO: 6 *or a combination of both*, wherein said peptide is immunochemically reactive with antibodies to the Epstein-Barr Virus VCA-p18 protein.

While Applicants have not explicitly provided the text from which the above amendment would find written description, it appears that what appears to provide support is found as discussed below:

The specification:

The description of "peptide 5" on page 22 is disclosed as being Combi-peptide of peptide 4 [SEQ ID NO: 6] and peptide 3 [SEQ ID NO: 5] linked by S-S-bridging, using extra cysteine residues at the C-terminus of peptide 4 and N-terminus of peptide 3, producing the peptide of the general formula:

H_2N-peptide 4 –S-S linkage via cysteine residues—peptide 3-COOH

In the Claims (as originally filed):

5. Peptide according to claim 4, comprising the amino acid sequence shown in SEQ ID NO: 5 *linked to* the amino acid sequences as shown in SEQ ID NO: 6.

6. Nucleic acid encoding a peptide according to any of claims 1-5.

The newly introduced claim, however, embraces a nucleic acid encoding a peptide comprising a combination of SEQ ID NO: 5 (peptide 3) and SEQ ID NO: 6 (peptide 4), which allows a nucleic acid encoding any number of amino acid (other than linkage provided by S-S bridging via extra cysteine residues) between peptide 4 and peptide 3, as well as a nucleic acid encoding peptide 3 linked at its C-terminus, peptide 4 by its N-terminus (i.e., reverse order), which clearly had not been disclosed nor contemplated.

For the above reasons, claims 32-34 are rejected as containing new matter.

- New Grounds – Necessitated by Amendment -

Applicants' amendment to claims 6-8 necessitates the following rejection.

Claims 23, 28, and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for amplification and detection of EBV virus nucleic acid sequence in a sample involving primer mediated amplification, wherein said primer is complementary to a region from SEQ ID NO: 1 and 3, does not reasonably provide enablement for the method of amplification and detection of EBV virus nucleic acid sequence involving the nucleic acids of claims 6-8 as currently recited. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation are summarized in In Re Wands (858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)). They include (A) the quantity of experimentation necessary, (B) the amount of direction or guidance presented, (C) the presence or absence of working examples, (D) the nature of the invention, (E) the state of the prior art, (F) the relative skill of those in the art, (G) the predictability or unpredictability of the art, and (H) the breadth of the claims.

(H) Breadth of the claims: the breadth of the claims involve a method of amplifying and detecting the presence of EBV nucleic acid in a sample with primers, wherein said primers are non-specific to EBV nucleic acids, as discussed below. The methods are directly dependent on the nucleic acids of claims 6-8.

Embodiment A) of claim 6 is drawn to a nucleic acid encoding ***any*** peptide that is reactive with antibodies which are reactive to VCA-p18 or VCA-p40 proteins, said ***any*** peptide comprising an immunoreactive fragment of the VCA-p18 or VCA-p40 proteins.

Thus, claim embraces any nucleic acid that encodes at least a fragment of a protein (which is one residue) that is in common with the VCA-p18 or VCA-p40 proteins, and said protein reacts with the recited antibody. Hence, if the antibody is a human antibody, said antibody would react with any protein that is from sources other than human, effectively embracing any nucleic acid encoding any protein, wherein the source of the protein is other than that which the antibody is generated/isolated from.

Embodiment B) of claim 6 is drawn to a functional variant of the above nucleic acid, which would fail under the same reasoning as the above. In addition, neither the Applicants nor one of skill in the art would be able to distinguish what nucleic acids are embraced by the instant

claims because the neither would know from which of the plurality of nucleic acids are functional variants, wherein the function is unknown.

Thus, the above genus of nucleic acid would not enable a skilled artisan to conduct the method of claim 23, that is, to amplify and detect the presence of EBV nucleic acid in a sample without undue experimentation since such primers would be non-specific.

Analogously, while claims 7 and 8 are drawn to a nucleic acid sequence comprising SEQ ID NO: 1 and 3 (respectively) or a *subsequence thereof*, wherein said subsequence encodes an EBV peptide comprising an *epitope* that is immunochemically reactive with antibodies to the EBV VCA-p18 protein, as already discussed above, any nucleic acid encoding a protein that is not from the same source from which the claimed antibody is generated/produced, would necessarily react with said antibody, thus inherently demonstrating the presence of an epitope.

Hence, it would also require undue experimentation of a skilled artisan to conduct the method of claims 28 and 29, for detecting the presence of EBV nucleic acid in a sample since the nucleic acids of claims 7 and 8 would be non-specific.

Therefore, for the above reasons, it would require undue experimentation of a skilled artisan to practice the invention commensurate in scope with the above claims.

Claim Rejections - 35 USC § 102

The rejection of claims 7, 8, 26, 27, 28, and 29 under 35 U.S.C. 102(b) as being anticipated by Ambinder et al. (Abstracts from Annual Meeting American Society of Microbiology, 1989, 89 Meet., 111, cited previously), made in the Office Action mailed on December 27, 2004 is withdrawn in view of the Amendment received on March 24, 2005.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 6, 9, 23, and 25 under 35 U.S.C. 102(b) as being anticipated by Ambinder et al. (Abstracts from Annual Meeting American Society of Microbiology, 1989, 89 Meet., 111, cited previously), made in the Office Action mailed on December 27, 2004 is maintained for the reasons of record.

Applicants' arguments presented in the Amendment received on March 24, 2005 have been fully considered but they are not found persuasive for the following reasons.

Applicants' arguments are addressed in the same order they were presented.

Applicants contend that claim 6 has been amended to delete the phrase, "at last part," and has been further amended to recite a nucleic acid encoding a peptide that specifically comprises an immunoreactive fragment of the VCA-p18 or VCA-p40 protein, or a functional variant thereof, which is immunoreactive with antibodies to VCA-p18 or VCA-p40.

Absent evidence to the contrary, the nucleic acid disclosed by Ambinder et al., which is different in sequences, (thus a variant), would necessarily react with the antibodies to the EBV VCA-p18 or VCA-p40 proteins.

According to *In re Best* 195 USPQ 430, 1997, the court stated that, "Patent Office can require applicant to prove that prior art products do not necessarily or inherently posses characteristics of his claimed product wherein claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes; burden

of proof is on applicant" (pp. 430). The nucleic acid encoded by Ambinder et al. is structurally different (thus, a variant). Whether the protein encoded by the nucleic acid of Ambinder et al. is not determinable as the PTO does not have the facility to conduct experiments. It is determined that the burden has been shifted to Applicants to provide contradicting evidence.

Therefore, Ambinder et al. would anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

The rejection of claims 30 and 31 under 35 U.S.C. 103(a) as being unpatentable over Ambinder et al. (Abstracts from Annual Meeting American Society of Microbiology, 1989, 89 Meet., 111, cited previously), made in the Office Action mailed on December 27, 2004 is withdrawn in view of the Amendment received on March 24, 2005.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m. The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (571) 272-0784. If the attempts to reach the above Examiners are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Young J. Kim
Patent Examiner
Art Unit 1637
6/6/2005

YOUNG J. KIM
PATENT EXAMINER

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